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Add new claim 28 as follows:

28) (New) The filter plate of claim 27 wherein the ultrafiltration filter has a first surface of the filter having a smaller pore size than the second surface.

#### REMARKS

Claims 1, 2, 4, 5, and 8 have been rejected under 35 USC 102(b) as being anticipated by Matkovich et al. (US 4,797,259). Applicants respectfully disagree.

The Office Action states that Matkovich discloses a 96 well filter citing column 1, lines 30-33. Applicants wish to point out that in the cited section, Matkovich mentions that 96 well devices had been used in the past but that they suffered from several disadvantages; their membranes were porous and therefore leaked under normal conditions due to gravity or capilliary action and they suffered from cross talk caused either by lateral migration through a sheet of membrane or the coalescing of pendant drops below the wells. Matkovich teaches away from using such devices.

The Office Action then states that the filter of Matkovich is adhered to the bottom of the well citing column 1, line 68 to column 2 line 5; column 3, line 34-37 and column 12, line 45-60. Column 1, line 68 to column 2 line 5 does not teach or suggest the use of adhesives. Rather it only says the membrane is placed against the bottom of the well. (column 2, line 2) Likewise column 3, line 34-37 fails to support the assertion. While it uses the word "adhered" it does not teach or suggest that the adhesion is created by an adhesive. Rather as is well documented throughout the text of the reference the use of heat or vibration welding is used to "adhere" the various layers together and then composite to each well. Additionally, the citation to column 12, line 45-60 does not support the allegation of adhesives. That cited portion states that the edges of the separate sheets may be adhered "such as by tacking or the like". Tacking is a heat or vibration weld applied to one or more positions to hold a material in place.

Applicants contend that Matkovich does not teach using an adhesive to bond a filter to the bottom of a multiple well plate as alleged by the Office Action. Rather it clearly teaches to one of ordinary skill in the art using a heat bonding to bond the various layers of filters together Appln Serial No. 09/\$\,\tag{304},304
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and to the wells of the plate. <u>See</u> Column 11, lines 23-24, "As a result of the heat process used,....", Column 11, lines 39-44; "Such a seal is typically accomplished by means of a heat, and preferably combined with pressure, treatment. Heat-sealing methods using radiant heat or ultrasonic sealing techniques with apparatus, such as heater blocks or welding horns, respectively, may be employed."; Column 12, lines 15-18, "Thus, each of the separate layers may be overlaid and the separate layers sealed to one another and to the bottom of each well in a single heat-sealing procedure.";Column 12, line 24, "Heat is then applied...."; Column 12, line 28, "Heat is applied...."; and Column 12, line 42, "....when heat is applied....".

Nowhere in the reference is the use of an adhesive mentioned. While Matkovich et al used the word adhere it is clear that they mean only adhesion caused by heat or melting of the various layers, not the use of a separate adhesive as is claimed in the present invention.

As the reference fails to teach the use of an adhesive to form a filter on the bottom of a plate as is required by Claim 1 any additional features of claims dependent on Claim 1 would also not be anticipated by the reference.

Likewise, the present invention uses a common sheet of filter material across the bottom of the plate and then uses the adhesive material to bond that sheet to the plate and to form impermeable walls between each well. This is unlike Matkovich et al which uses individual membrane pieces heat bonded to the periphery of each well. They do this to avoid the cross talk issue that occurred in the past. Matkovich et al fails to teach or suggest this element of the claimed invention and therefore the claims are not anticipated by the reference.

Claim 6 has been rejected under 35 USC 103(a) as obvious over Matkovich et al. It is stated that the reference teaches a plurality of wells but fails to teach 384 well plates. The Office Action then states that it would have been obvious that a 384 well format is only a further replication of a plurality of wells. As discussed at page 3, lines1-7 of the present invention, the ability to effectively seal 384 individual membrane pieces to 384 well bottoms as would be required by the reference would be time consuming and impracticable, if not impossible. Applicants have provided an alternative means for accomplishing this feat in a simple and efficient manner. It would not have been obvious to one of ordinary skill in the art that the reference could be used with 384 wells in view of the above.

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Claims 1, 2, 7, 10, 11, 13, 16, and 17 have been rejected under 35 USC 103(a) as obvious over Clark in view of Cole et al. Applicants disagree.

The Office Action states that Clark doesnot teach the use of an adhesive to seal the membrane to the bottom of the well. Cole et al is cited as it is purported to teach the use of an adhesive to seal a membrane to the bottom of each well and that it would have been obvious to use the adhesive of Cole et.al. to seal the membrane to Clark due to its use of any conventional bonding method.

There is no motivation in the two references to suggest their combination. They relate to different devices (a filtration plate vs a transfer plate and the problem of assay testing (Cole et al) vs. recovering the filter with the filtrate intact (Clark)).

The suggested combination would not have taught or suggested the present invention as neither reference teaches or suggests using an adhesive to bond the filter to the plate. Rather only Cole et. al. relates to the bonding of filters to each individual well while Clark uses an adhesive to bond the filter to the adhesive and either a nonporous foil or a closed non-porous depression. Neither one, alone or in combination, suggest the use of the adhesive as in claim 1 to bond a single piece of filter across the bottom of the plate. Clark needs individual filter pieces in order to recover them easily. Cole et. al. relates to an assay system and uses individual membranes on each well. The reason is not stated for this in Cole et.al.

Claims 24, 25 and 26 have been indicated as being allowable.

New claims 27 and 28 have been added to cover one preferred embodiment of the present invention. This embodiment uses an ultrafiltration membrane in combination with a 384 well plate. This embodiment has been and continues to be used by researchers, such as deCode Genetics, for the rapid and high throughput screening of genomic products such as disease-gene research. A copy of a May 23, 2001 press release by deCode and Millipore is attached for the examiner's reference.

It is believed that the invention of claims 27 and 28 are novel and unobvious over the cited art for the same reasons cited above with the other claims pending in this application. In addition, the prior art does not teach or suggest a plate having an ultrafiltration membrane

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sheet adhered to the bottom of a 384 well plate nor an ultrafiltration membrane with different pore sizes on its opposite surfaces.

Applicants believe this reply is complete and conforms to the requirements of the Office Action. Applicants' attorney requests that the Examiner call him if it is believed that this reply is not in complete compliance with any of the Office Action's requirements.

Respectfully Submitted,

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#### CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to Assistant Commissioner of Patents, Washington D.C. 20231

On May 13 2003

Kimberly Atwood

Typed name of person signing

Phillip Clark,et al. 09/844,304 April 27, 2001 Multiple Well Plate with Adhesive Bonded Filter

## Version Marked to Show Changes Made

Claims 4 and 8 have been cancelled.

New claim 27 has been added as follows:

27. (New) A multi well filter plate for filtering a liquid comprising,

a plate having top and bottom surfaces,

384 holes passing through said plate,

an ultrafiltartion filter having a first and second surface,

said first surface of said filter being sealed to said bottom surface of said plate,

said seal being an adhesive,

said seal being liquid tight so that when a sample is placed in said holes and a pressure differential is applied between said top and bottom surfaces the liquid passes through said filter.

New claim 28 has been added as follows:

28) (New) The filter plate of claim 27 wherein the ultrafiltration filter has a first surface of the filter having a smaller pore size than the second surface.





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PROPRIETS

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## deCODE genetics Supports High-throughput Disease-gene Research with Millipore's MultiScreen384 Purification Platform

Reykjavik, ICELAND and Bedford, MASSACHUSETTS, May 23, 2001 deCODE genetics (Nasdaq/Nasdaq Europe:DCGN) and Millipore Corporation (NYSE/MIL) today announced that deCODE has selected Millipore's MultiScreen™384 platform to purify their samples prior to DNA sequencing.

Based in Reykjavik, deCODE utilizes Iceland's unique genealogical resources to conduct population-wide DNA linkage analyses to identify the inherited causes of common diseases. "We operate one of the highest-throughput disease-gene research operations in the world," says Dr. Jeff Gulcher, deCODE's Vice President for Research and Development, "and we are able to focus our sequencing on small regions of the genome specifically linked to disease. But with more than 40 disease programs underway, we need our sequencing to be highly efficient and to yield the most accurate data possible. The Millipore384-well platform fits our high-throughput model and gives us very clean DNA."

Millipore's MultiScreen384 platform is a new, high-throughput membrane-based system for biomolecular separations. Based upon a size exclusion technology, the MultiScreen384 platform is automation-compatible, making it an ideal sample preparation method for the high throughput demands of the world's leading genomics centers.

# About deCODE genetics

deCODE genetics (www.decode.com), based in Reykjavik, Iceland, is conducting research into the inherited causes of common diseases. Through its population-based approach and three main business units providing disease-gene and drug target identification, database services and informatics tools, deCODE is turning raw genomics data into products and services for the healthcare industry.

## **DeCode Forward Looking Statement**

Any statements contained in this press release that relate to future plans, events or performance are forward-looking statements that involve risks and uncertainties including, but not limited to, those relating to technology and product development, market acceptance, government regulation and regulatory approval processes, intellectual property rights and litigation, dependence on strategic partners, ability to obtain financing, competitive products and other risks identified in deCODE's filings with the Securities and Exchange Commission. Actual results, events or performance may differ materially. deCODE undertakes no obligation to publicly release any revisions to these forward-looking statements resulting from events or circumstances after the date hereof.

### **About Millipore**

Millipore is a multinational, high technology company that applies its purification technology to critical research and manufacturing applications in the biosciences and microelectronics industries. In biosciences, Millipore provides technologies, tools and services for the development and production of new therapeutic drugs. For more information visit, www.millipore.com. In microelectronics, Millipore provides products, components and services for the production of semiconductor devices. For more information visit, www.mykrolis.com.

### Millipore Forward Looking Statement Disclaimer

The matters discussed herein, as well as in future oral and written statements by management of Millipore Corporation that are forward-looking statements, are based on current management expectations that involve substantial risks and uncertainties which could cause actual results to differ materially from the results expressed in, or implied by, these forward-looking statements. Potential risks and uncertainties that could affect Millipore's future operating results include, without limitation, difficulties in the successful separation of the biosciences and microelectronics businesses; difficulties in the successful implementation of our restructuring activities; foreign exchange rates; increased regulatory concerns on the part of the biopharmaceutical industry; further consolidation of drug manufacturers; competitive factors such as new membrane technology, and/or a new method of chip manufacture which relies less heavily on purified chemicals and gases; availability of raw materials or component products on a timely basis; inventory risks due to shifts in market demand; change in product mix; conditions in the economy in general, and in the biosciences and microelectronics markets in particular; potential environmental liabilities; the inability to utilize technology in current or planned products due to overriding rights by third parties; difficulties inherent in research and development activities; and the risk factors listed from time to time in Millipore's filings with the SEC.

Contact:

deCODE genetics

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